Appendix

1. A method of treating a patient with a disease wherein the patient contains diseased cells which cells contain, or are associated with, an abnormal molecule or abnormally elevated amount of a molecule and which cells are capable of presenting at least part of the molecule on their surface by an HLA class I (or equivalent) molecule, the method comprising administering to the patient a therapeutically effective amount of cytotoxic T lymphocytes (CTL) which recognise at least part of the molecule when presented by an HLA class I (or equivalent) molecule on the surface of a cell characterised in that the cytotoxic T lymphocytes are derived from an individual which individual does not carry the HLA class I (or equivalent) molecule type which, in the patient, presents at least part of the abnormal molecule, or molecule abnormally elevated, contained in or associated with the diseased cells of the patient.

2. A method according to Claim 1 wherein the CTL are a clonal population of CTL.

3. A method according to Claim 1 wherein the CTL are substantially free of other cell types.

4. A method according to Claim 1 wherein the molecule is a polypeptide.

5. A method according to Claim 4 wherein the polypeptide is a mutuant polypeptide associated with the diseased cells.

6. A method according to Claim 4 wherein the polypeptide is present at a higher level in the diseased cells compared to non-diseased cells.

7. A method according to Claim 1 wherein the disease is a cancer.

8. A method according to Claim 7 wherein the cancer is any one of breast cancer; bladder cancer; lung cancer; prostrate cancer; thyroid cancer; leukaemias and lymphomas such as CML, ALL, AML, PML; colon cancer; glioma; seminoma; liver cancer; pancreatic cancer; bladder cancer; renal cancer; cervical cancer; testicular cancer; head and neck cancer; ovarian cancer; neuroblastoma and melanoma.

9. A method according to Claim 1 wherein the disease is caused by a chronic viral infection.

10. A method according to Claim 9 wherein the virus is any one of HIV, papilloma virus, Epstein-Barr virus, HTLV-1, hepatitis B virus, hepatitis C virus and herpes virus.

11. A method according to Claim 10 wherein the virus is HIV.

12. A method according to Claim 1 wherein the disease is associated with an abnormally elevated amount of a hormone.

13. A method according to Claim 1 wherein the disease is a bacterial disease caused by a chronic bacterial infection.

14. A method according to Claim 1 further comprising the step of determining the HLA class I (or equivalent) molecule type of the patient prior to administration of the CTL.

15. A method according to Claim 14 wherein the type is determined using DNA typing.

16. A method according to Claim 1 wherein the patient is human.

17. A method according to Claim 14 wherein the cytotoxic T lymphocyte is selected from a library of CTL clones, the library comprising a plurality of CTL clones

derived from individuals with differing HLA class I (or equivalent) molecule type and each CTL clone recognises the diseased cells.

18. A method according to Claim 17 wherein each CTL clone recognises at least part of the same molecule contained in or associated with the diseased cells.

20. A method of making a clonal population of cytotoxic T lymphocytes (CTL) reactive against a selected molecule the method comprising the step of (a) co-culturing a sample containing CTL or a precursor thereof derived from a healthy individual with a stimulator cell which expresses HLA class I (or equivalent) molecules on its surface and that represents at least a part of the selected molecule in a large proportion of occupied HLA class I (or equivalent) molecules present on the surface of the stimulator cell and (b) selecting a CTL clone reactive against the selected molecule when at least a part of the molecule is presented by an HLA class I (or equivalent) molecule on the surface of a cell, wherein the healthy individual does not carry the HLA class I (or equivalent) molecule type which, on the stimulator cell, presents at least a part of the selected molecule.

21. A method according to claim 20 wherein the sample containing CTL or a precursor thereof is PBMC.

22. A method according to Claim 20 wherein the molecule is a polypeptide.

23. A method according to Claim 20 wherein the selected molecule is an abnormal molecule associated with a diseased cell, or a molecule associated with a diseased cell wherein an abnormally elevated amount of the molecule is present in the diseased cell.

24. A method according to Claim 23 wherein the selected molecule is a mutuant polypeptide associated with a diseased cell or a polypeptide present at a higher level in the diseased cell compared to a non-diseased cell.

25. A method according to Claim 23 wherein the diseased cell is any one of a cancer cell, a virus-infected cell, a bacterium infected cell and a cell expressing an abnormally elevated amount of a hormone.

26. A method according to Claim 20 wherein the healthy individual is a human.

27. A method according to Claim 26 wherein the selected molecule is any one of cyclin D1, cyclin E, mdm 2, EGF-R, erb-B2, erb-B3, FGF-R, insulin-like growth factor receptor, Met, myc, p53, BCL-2, ie mutant Ras, mutant p53, a polypeptide associated with the BCR/ABL translocation in CML and ALL, mutant CSF-1 receptor, mutant APC, mutant RET, mutant EGFR, a polypeptide associated with PML/RARA translocation in PML, a polypeptide associated with E2A-PBX1 translocation in pre B leukaemias and in childhood acute leukaemias, human papilloma virus proteins, Epstein-Barr virus proteins, HTLV-1 proteins, hepatitis B or C virus proteins, herpes-like virus proteins and HIV encoded proteins.

28. A method according to Claim 20 further comprising determining the HLA Class I (or equivalent) type of the healthy individual.

29. A method according to Claim 28 wherein the HLA class I (or equivalent) type is determined by DNA analysis.

30. A method according to Claim 20 wherein the stimulator cell has a type of HLA class I (or equivalent) molecule on its surface which HLA class I (or equivalent) molecule type is not present in the healthy individual.

31. A method according to Claim 20 wherein the stimulator cell is a cell which is substantially incapable of loading the HLA class I (or equivalent) molecule with at least a part of the selected molecule.

32. A method according to Claim 31 wherein the cell is a mammalian cell defective in the expression of a peptide transporter.

33. A method according to Claim 32 wherein the mammalian cell lacks or has a reduced level of the TAP peptide transporter.

34. A method according to Claim 31 wherein the cell is an insect cell.

35. A method according to Claim 34 wherein the cell is a *Drosophila* cell.

36. A method according to Claim 20 wherein the stimulator cell is a host cell transfected with a nucleic acid molecule capable of expressing the HLA class I (or equivalent) molecule.

37. A method according to Claim 36 wherein the host cell before transfection expresses substantially no HLA class I (or equivalent) molecules.

38. A method according to Claim 20 wherein the stimulator cell expresses a molecule important for T cell costimulation.

39. A method according to Claim 38 wherein the molecule important for T cell costimulation is any of B7.1, B7.2, ICAM-1 and LFA3.

40. A method according to Claim 20 wherein substantially all the HLA class I (or equivalent) molecules expressed on the surface of the stimulator cell are of the same type.

41. A clonal population of cytotoxic T lymphocytes reactive against a selected molecule obtainable by the method of Claim 20.

42. A clonal population of cytotoxic T lymphocytes according to Claim 41 for use in medicine.

43. A pharmaceutical composition comprising a clonal population of cytotoxic T lymphocytes reactive against a selected molecule according to Claim 41 and a pharmaceutically acceptable carrier.

45. A library of CTL clones, the library comprising a plurality of CTL clones derived from individuals and each CTL clone is restricted by a different HLA class I allele and recognises a molecule associated with a selected disease.

46. A therapeutic system comprising (a) means to determine the HLA class I (or equivalent) type of a patient to be treated and (b) a library of CTL clones as defined in Claim 45.

47. A method of making a cytotoxic T lymphocyte (CTL) suitable for treating a patient, the method comprising making a clonal population of CTL by the method of Claim 20; preparing a genetic construct capable of expressing the T-cell receptor (TCR) of the clonal population of CTL, or a functionally equivalent molecule; and introducing the genetic construct into a CTL or precursor thereof which CTL or precursor is derived from the patient.

48. A cytotoxic T lymphocyte suitable for treating a patient obtainable by the method of Claim 47.

49. A method of treating a patient with a disease wherein the patient contains diseased cells which cells contain, or are associated with, an abnormal molecule or an abnormally elevated amount of a molecule and which cells are capable of presenting at least part of the molecule on their surface by an HLA class I (or equivalent) molecule, the method comprising administering to the patient a therapeutically effective amount of cytotoxic T lymphocytes (CTL) which recognise at least part of the molecule when presented by an HLA class I (or equivalent) molecule on the surface of a cell wherein the CTL is a CTL according to Claim 48.